



Comparison of energy cost between genders during treadmill walking at a self-selected pace

Kleverton Krinski^{1*}, Hassan Mohamed Elsangedy¹, Maressa Priscila Krause², Luciana da Silva Timossi¹ and Sergio Gregorio da Silva¹

¹Departamento de Educação Física da Universidade Federal do Paraná, Rua Coração de Maria, 92, 80215-370, Curitiba, Paraná, Brazil.

²Departamento de Educação Física da Universidade Tecnológica Federal do Paraná Rebouças, Curitiba, Paraná, Brazil. *Author for correspondence. E-mail: klevertonkrinski@hotmail.com

ABSTRACT. The purpose of this study was to compare the energy cost between genders during treadmill walking at self-selected pace; and to verify if the energy cost achieve the values recommended for weight maintenance or loss proposed by the American College of Sports Medicine (ACSM). Seventeen men and seventeen women, mean age of 23.32 ± 3.06 years, undertaken two experimental sessions: (I) anthropometric measurements and a load-incremental maximum test; and, (II) a 20-min walking test at self-selected pace on treadmill. Men showed a greater energy cost than women (146.18 ± 47.66 and 100.86 ± 17.04 kcal, respectively). This difference was maintained after adjust by body weight (2.2 ± 0.5 and 1.7 ± 0.2 kcal kg^{-1} , respectively). The greater energy cost found in men can be explained by the self-selected treadmill speed that lead to a greater $\dot{V}\text{O}_2$ in men. However, the exercise intensity selected by both genders did not elicit an effective energy cost that can promote weight maintenance or loss. Nonetheless, if participants performed a longer walking (> 20 minutes), they probably would achieve the energy cost recommended by the ACSM guidelines.

Keywords: exercise, men, women, energy expenditure.

Comparação do gasto energético entre os gêneros durante a caminhada na esteira em ritmo autoselecionado

RESUMO. O objetivo do presente estudo foi comparar o gasto energético entre os gêneros durante a caminhada na esteira em ritmo auto-selecionado e verificar se a intensidade que os sujeitos buscam caminhar promove um dispêndio energético dentro do recomendado para a manutenção e/ou redução do peso corporal conforme proposto pelas diretrizes do ACSM. Participaram 17 homens e 17 mulheres com média de idade de $23,32 \pm 3,06$ anos, submetidos a duas sessões experimentais: (I) avaliação antropométrica e teste incremental máximo, e (II) um teste de 20 minutos de caminhada na esteira em ritmo auto-selecionado. Os homens apresentaram um gasto energético superior ao das mulheres ($146,18 \pm 47,66$ e $100,86 \pm 17,04$ kcal, respectivamente). Essas diferenças persistiram após correção da massa corporal ($2,2 \pm 0,5$ e $1,7 \pm 0,2$ kcal kg^{-1} , respectivamente). Pode-se concluir que o maior gasto energético encontrado nos homens, foi decorrente da velocidade de caminhada auto-selecionada, proporcionando um $\dot{V}\text{O}_2$ superior. Contudo a intensidade de caminhada selecionada por ambos os gêneros não foi suficiente para propiciar um gasto energético considerado efetivo para manutenção e/ou redução do peso corporal. Entretanto, é possível especular que se a atividade fosse realizada por um período mais longo (> 20 minutos), os indivíduos poderiam atingir as diretrizes propostas pelo ACSM.

Palavras-chave: exercício, homens, mulheres, dispêndio energético.

Introduction

Walking is the activity more frequently performed by active and sedentary men and women, whose wish maintain and/or reduce body weight, which may be due its easy accessibility, safety, simplicity, popularity, and offer a tolerable intensity and easily regulated (ACSM, 2006; SIEGEL et al., 1995; WILLIAMS et al., 2008). However, for this activity become adequate for weight control, healthy professionals should to measure accurately its energy cost (BROWNING et al., 2006).

The American College of Sports and Medicine recommended that energy cost from physical exercise achieve a range of 150 to 400 kcal per day, when the purpose to maintain or reduce body weight (ACSM, 2006). Although be unquestionable the need for a minimum energy cost during exercise for promote body weight maintenance, Cox et al. (2003) and Dishman et al. (1994), showed that adults have a tendency to exercise at a self-selected intensity, considered as preferred, than an intensity previously prescribed. According to Emmons and

Diener (1986), the reason for individuals selected a different intensity than that prescribed may be related to the fact the individual want to perform something that is pleasurable, and avoid those situations related to discomfort or unpleasant experiences.

Although the self-selection of exercise intensity be a strategy used with the purpose to become its practice more pleasant, there is a lack of studies regarding the energy cost from walking at self-selected intensity in men and women. Previous investigations (LEICHT; CROWTHER, 2007; LOFTIN et al., 2010) purposed to compare the energy cost between genders were based on protocols with prescribed intensity, then it is necessary to broaden these knowledge's during an intensity that the individual prefers to perform. For this reason, the present study purposed to compare the energy cost between genders during walking at self-selected pace, and to verify if the intensity self-selected is enough to elicits the energy cost recommended for maintenance and/or reduction of body weight as proposed by the ACSM guidelines (ACSM, 2006).

Material and methods

Sample

The sample size was calculated by using the software GPower 3.0; taking into consideration the comparisons through independent t-test, with alfa level of 0.05 and effect size of 1.17; which estimated the need for 17 subjects in each experimental group. All subjects had previous experience to walk on a treadmill, and they were classify as physically active by the IPAQ (International Physical Activity Questionnaire - short version) (MATSUDO et al., 2001). The subjects undertaken a anamneses (medical history) indicating that they were apparently healthy, non-smoking, were not under a restrictive diet, and showed a stabilization of body weight from the last three months prior to be included in the study. Furthermore, subjects reported do not take any medication known to influence metabolic or cognitive functions. All women were a regular menstrual cycle (25 to 32 days), and were not under oral contraceptives six months prior to be included in the study.

The information's regarding the study procedures, possible benefits and risks were explained individually to the subject, and then the subject signed the informed consent form voluntarily. The study protocol was approved by the Institutional Ethic Committee of the Federal University of Paraná (CEP/SD:829.164.09.10).

Procedures

The experimental sessions were conducted between 9 and 12 AM with the purpose to avoid circadian variation, under similar environmental conditions (21°C and 55% relative humidity), and with a minimum of 48 hour between sessions. Participants were instructed to refrain from vigorous exercise 24 hours prior to the tests, caffeine-containing products, and any meal 2 hours before the exercise trials.

Anthropometrics measurements of body mass (BM, kg - scale: Toledo 2096), height (H, cm - stadiometer: Sanny, Standard), and Body Mass Index (BMI, kg cm⁻²) were obtained according with procedures proposed by Gordon et al. (1988). Body density (g cm⁻³) was calculated based on equation proposed by Durnin and Womersley (1974), using the skinfold method (biceps, triceps, subscapular, suprailiac), and then body fat (%Fat) was calculated by Siri equation (1961). All measurements were done by a single staff member with the purpose to avoid inter-evaluator variations.

Heart rate was measured by a cardiofrequencimeter (Polar Oy model Sports Tester, Kempele, Finland). Oxygen consumption ($\dot{V}O_2$) was obtained breath-by-breath, using a computerized spirometry system of open-circuit (Cosmed K4b², Roma, Itália), which includes a gases analysis unit, battery, face-mask, and heart monitor. Prior to each test, the metabolic system was calibrated (Hans Rudolph, model 5530, Kansas City, Missouri, USA). Data was recorded from the mean values of breath-by breath in each 15-s.

The maximal oxygen uptake ($\dot{V}O_{2Max}$) was determined by the highest $\dot{V}O_2$ value (mean of 1 minute interval) obtained during the last completed stage of the incremental treadmill test (CAIOZZO et al., 1982). Additionally, it was required at least two of the following criteria to consider that maximal oxygen uptake was attained: (a) $\dot{V}O_2$ plato, indicated by a difference of < 150 mL min.⁻¹, (b) a respiratory exchange ratio of ≥ 1.10 and (c) heart rate within ± 10 bpm of age-predicted HR_{max}. Maximal heart rate (HR_{max}), was determined by the highest HR value (mean of 1 minute interval) verify in the last completed stage of the incremental treadmill test.

All participants underwent to an incremental test until exhaustion on a treadmill (Reebok Fitness, mode: X-fit 7, London, United Kingdom). This experimental session was initiated with a 5 minutes warm-up, at a standard speed of 4.0 km h⁻¹, without grade. Next, the incremental test was conducted by using the Bruce protocol (BRUCE et al., 1973). The test remained until exhaustion volitional of the subject. All subjects were verbally encouraged to continue the exercise for

as longer as possible. Maximal oxygen uptake and heart rate were measured throughout the test.

After a 48 hours interval, participants performed the 20 minutes walking test at self-selected pace on a treadmill. Subjects were instructed to self-select a treadmill speed according to the procedures proposed by Ekkekakis and Lind (2006). Subjects were allowed to make these adjustments during the first minute of the test, and then at 00:05, 00:10, and 00:15 by using the speed control on the treadmill. The treadmill panel was covered for avoiding that the subject was influenced by the actual speed as recommended by Pintar et al. (2006).

The energy cost (EC) was determined by using the data from the indirect calorimetric (spirometry system). This method is based on oxygen uptake ($\dot{V}O_2$) and carbon dioxide production ($\dot{V}CO_2$) analysis which determined the respiratory quotient ($RQ = \dot{V}O_2/\dot{V}CO_2$), it calculated the amount of energy required for the metabolic processes (MELLO et al., 2008). This data was obtained from the 20-min. of walking at a self-selected pace. This procedure allow 3-min. for the subject achieve the steady-state (non-significant increases on $\dot{V}O_2$ during the last 2-min. and a $RQ < 1.0$, indicating that the energy source was primarily supplied by the oxidative metabolism). The RQ was used for calculating the caloric equivalent non-proteic per liter of oxygen uptake during the exercise, as a result, it was obtained the energy cost in kilocalories (kcal) according to the equation proposed by Weir (1949).

Statistical Procedures

The statistical analysis used measurement of central tendency and variability. The Kolmogorov-Smirnov was used to test the normality of the data. The differences between genders were analyzed by the Student *t* test for independent samples, for the following variables: age, body mass, height, BMI, %Fat, HR max, $\dot{V}O_{2Max}$ and energy cost of the 20-min. walking at self-selected pace. The effect size (*d*) was reported for each comparison as recommended by Cohen (1992). All statistical analysis was calculated by using the Statistical Package for the Social Sciences (SPSS, version 13.0) for Windows, with a $p \leq 0.05$.

Results

Subjects demographic, anthropometric and physiological characteristics are shown on Table 1. The *t* test indicated that men had a higher stature and body mass than women ($p \leq 0.05$); however, a lower percentage of fat ($p \leq 0.05$). Additionally, men had a greater cardiorespiratory fitness (ACR) indicating by their $\dot{V}O_{2Max}$. According to the ACSM (2006) criteria, this sample can be categorized as a good conditioning level due its $\dot{V}O_{2max}$ mean values, which was above the 90 percentile for men (57.38 mL kg⁻¹ min.⁻¹) and above the 80 percentile for women (45.95 mL kg⁻¹ min.⁻¹), based on the age group classification (20 to 29 years-old).

Physiological parameters from the 20-min. of walking at a self-selected pace are show on Table 2.

Table 1. Subjects demographic, anthropometric and physiological characteristics.

	General		Men		Women		P	d
	Mean	SD	Mean	SD	Mean	SD		
Age (years)	23.32	3.06	24.05	3.32	22.58	2.67	0.16	0.50
Body mass (kg)	65.39	10.75	71.96	10.15	58.81	6.59	0.01*	1.58
Weigth (cm)	1.68	0.09	1.75	0.06	1.62	0.06	0.01*	2.23
BMI (kg cm ⁻²)	22.77	2.10	23.31	2.21	22.23	1.89	0.13	0.54
% Fat	19.67	3.57	18.38	3.20	20.88	3.55	0.42	0.76
HR _{Max} (bpm)	190.0	6.19	189.8	5.45	190.1	7.01	0.91	0.04
$\dot{V}O_{2Max}$ (mL kg ⁻¹ min. ⁻¹)	51.66	8.13	57.38	5.92	45.95	5.63	0.00*	2.04

Mean \pm SD. BMI: Body mass index; % Fat: percentage of body fat; HR_{max}: Maximal heart rate; $\dot{V}O_{2max}$: Maximal oxygen consumption. *Difference between men and women ($p \leq 0.05$).

Tabela 2. Características demográficas, antropométricas e fisiológicas dos sujeitos.

	General		Men		Women		P	D
	Mean	SD	Mean	SD	Mean	SD		
$\dot{V}O_2$ (mL kg ⁻¹ min. ⁻¹)	19.79	4.53	21.27	5.52	18.30	2.70	0.05*	0.70
% $\dot{V}O_{2max}$	38.94	9.15	37.54	10.75	40.34	7.27	0.38	0.31
Speed (m seg ⁻¹)	1.58	0.17	1.65	0.18	1.50	0.12	0.01*	1.01
EC (kcal)	123.5	42.1	146.1	47.6	100.8	17.1	0.01*	1.40
EC (kcal kg ⁻¹)	1.8	0.4	2.2	0.5	1.7	0.2	0.04*	1.45
EC (J Kg ⁻¹ m ⁻¹)	4.56	0.81	4.28	0.89	4.84	0.73	0.05*	0.70

Mean \pm SD. $\dot{V}O_2$: Oxygen consumption; % $\dot{V}O_{2max}$: Percentage of maximal oxygen consumption; EC: Energetic cost. *Difference between men and women ($p \leq 0.05$).

During the walking at self-selected pace, performed on a treadmill, was verified a greater energy cost in men than in women, (146.18 ± 47.66 and 100.86 ± 17.04 kcal, respectively), even after body mass adjustment (2.2 ± 0.5 and 1.7 ± 0.2 kcal kg^{-1} respectively). Also, it was observed that walking speed (1.65 ± 0.18 and 1.50 ± 0.12 m s^{-1}) and the $\dot{V}\text{O}_2$ (21.2 ± 5.5 and 18.3 ± 2.7 $\text{mL kg}^{-1} \text{min}^{-1}$) were greater in men.

Discussion

Walking is a popular exercise modality and its is recommended for general population. However, less is known about the differences on the energy cost between genders during a self-selected pace session, and if the intensity selected is effective for promoting an energy cost recommended by the ACSM (2006) for weight maintenance or weight loss.

The results from the present study shown that during a 20-min of walking at self-selected pace, men had a energy cost equivalent to 146.18 ± 47.66 kcal, greater than found in women 100.86 ± 17.04 kcal. These findings are in agreement with Butts et al. (1995), who's evaluated 29 men and 37 women, and reported a higher energy cost in men. However, there was performed at three different exercise intensities during the walking, and the intensity was previously prescribed at 0.89, 1.34 and 1.79 m s^{-1} . On the other hand, Kravitz et al. (1997), is one of the few studies that compared the energy cost between genders during walking at a self-selected pace, found similar results to the present study, in which the greater energy cost was found in men.

The greater energy cost found in men may be related to the differences on body mass that can influence the energy cost of a bear weight exercise, such as walking (McARDLE et al., 2006). Nonetheless, when this values were adjusted for body mass (kcal kg^{-1}), the genders differences was not significant. The differences found can be result of the walking speed selected by men, which was superior women, (1.65 ± 0.18 and 1.50 ± 0.12 m s^{-1} , respectively). Similarly, Finley and Cody (1970) shown that men prefer walking a superior speed than women (1.37 and 1.23 m s^{-1} , respectively). A possible reason for this difference can be related to the greater cardiorespiratory fitness (CRF), as reported recently by Krinski et al. (2009).

Consequently of the higher walk speed selected, men had a greater $\dot{V}\text{O}_2$ than women (21.27 ± 5.52 e 18.30 ± 2.70 $\text{mL kg}^{-1} \text{min}^{-1}$, respectively), leading to a higher metabolic demand that contribute to the energy cost during the 20-min. walking at a self-

selected pace. Although men had a higher energy cost, both genders self-selected an intensity of $38\% \dot{V}\text{O}_{2\text{max}}$, promoting en energy cost of 123.5 ± 42.1 kcal. This energy cost is below the recommendation proposed by the ACSM (2006) for body weight maintenance or loss, which target energy cost of 150 a 400 kcal per exercise session. In the same way Spelman et al. (1993) conducted a study with men and women, aged between 22 and 58 years-old, who walked regularly, showing that the energy cost was 91.5 kcal during 15-min. of walking at a self-selected pace. Even though this energy cost be inferior to that found in this study, if the energy cost is calculated for 20-min. of walking, instead of 15-min., the result will be approximately of 122 kcal, which is similar with our results.

Although the energy cost found is below to the recommendations, it possible to hypothesize that if the activity is performed longer, it could promote a higher energy cost, and consequently weight maintenance or loss. According with, Anjos et al. (2008), a walking performed at 1.12 m seg^{-1} , needs around 46 minutes for achieve the energy cost recommended. In the present study the mean speed was, 1.58 m s^{-1} , superior to that found by Anjos et al. (2008), suggesting that the subjects could achieve the energy cost recommended in a lower time.

From this perspective, future investigations may used longer periods for clarify this hypothesis. In addition, our findings must be analyzed cautiously, because it may be not generalized by other population (subject with different age, sedentary, athletes, and special health condition and obese).

Conclusion

The results found in the present study have theoretic and practical applications. From a theoretic perspective, men had a greater energy cost than women. The higher walking speed self-selected and the greater $\dot{V}\text{O}_2$ that lead to a greater energy cost. At practical application, it was verify that independently of gender, younger active individuals self-selected a walk intensity during the 20-min. below that recommended by the ACSM for weight maintenance or loss. However, it is necessary to take into consideration that if the walking was performed for longer period, these individuals probably could achieve the energy cost recommended.

References

ACSM-American College of Sports Medicine. **ACSM's Guidelines for Exercise Testing and Prescription**, 7th ed. Baltimore: Lippincott Williams and Wilkins, 2006.

- ANJOS, L. A.; WAHRLICH, V.; BOSSAN, F. M.; SALIES, M. N.; SILVA, P. B. Energy expenditure of walking at different intensities in Brazilian college women. **Clinical Nutrition**, v. 27, n. 1, p. 121-125, 2008.
- BROWNING, C. R.; BAKER, E. A.; HERRON, J. A.; KRAM, R. Effects of obesity and sex on the energetic cost and preferred speed of walking. **Journal of Applied Physiology**, v. 100, n. 2, p. 390-398, 2006.
- BRUCE, R. A.; KASUMI, F.; HOSMER, D. Maximal oxygen intake and nomographic assessment of functional aerobic impairment in cardiovascular disease. **American Heart Journal**, v. 85, n. 4, p. 546-562, 1973.
- BUTTS, N. K.; KNOX, K. M.; FOLEY, T. S. Energy costs of walking on a dual-action treadmill in men and women. **Medicine and Science in Sports and Exercise**, v. 27, n. 1, p. 121-125, 1995.
- CAIOZZO, V. J.; DAVIS, J. A.; ELLIS, J. F.; AZUS, J. L.; VANDAGRIFF, R.; PRIETTO, C. A.; McMASTER, W. C. A comparison of gas exchange indices used to detect the anaerobic threshold. **Journal of Applied Physiology**, v. 53, n. 5, p. 1184-1189, 1982.
- COHEN, J. A power primer. **Psychology Bulletin**, v. 112, n. 1, p. 155-159, 1992.
- COX, K. L.; BURKE, V.; GORELY, T. J.; BEILIN, L. J.; PUDDEY, I. B. Controlled comparison of retention and adherence in home versus center-initiated exercise interventions in women ages 40-65 yr: The SWEAT study. **Preventive Medicine**, v. 36, n. 1, p. 1087-1094, 2003.
- DISHMAN, R. K.; FARQYHAR, R. P.; CURETON, K. J. Responses to preferred intensity of exercise in men differing in activity level. **Medicine and Science in Sports and Exercise**, v. 26, n. 1, p. 783-790, 1994.
- DURNIN, J. V.; WOMERSLEY, J. Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. **British Journal of Nutrition**, v. 32, n. 1, p. 77-97, 1974.
- EKKEKAKIS, P.; LIND, E. Exercise does not feel the same when you are overweight: the impact of self-selected and imposed intensity on affect and exertion. **International Journal of Obesity**, v. 30, n. 4, p. 652-660, 2006.
- EMMONS, R. A.; DIENER, E. A goal-effect analysis of everyday situational choices. **Journal of Research in Personality**, v. 20, n. 3, p. 309-326, 1986.
- FINLEY, F. R.; CODY, K. A. Locomotive characteristics of urban pedestrians. **Archives of Physical Medicine and Rehabilitation**, v. 51, n. 7, p. 423-426, 1970.
- GORDON, C. C.; CHUMLEA, W. C.; ROCHE, A. F. Stature, recumbent length and weight. In: LOHMAN, T. G.; ROCHE, A. F.; MARTORELL, R. (Ed.). **Anthropometric standardization reference manual**. Champaign: Human Kinetics Books, 1988. p. 3-8.
- KRAVITZ, L.; ROBERGS, R. A.; HAYWARD, V. H.; WAGNER, D. R.; POWERS, K. Exercise mode and gender comparisons of energy expenditure at self-selected intensities. **Medicine and Science in Sports and Exercise**, v. 29, n. 8, p. 1028-1035, 1997.
- KRINSKI, K.; SILVA, S. G.; ELSANGEDY, H. M.; COLOMBO, H.; BUZZACHERA, C. F.; SANTOS, B. V.; COELHO, R. W.; CAMPOS, W. Respostas fisiológicas durante a caminhada na esteira em ritmo auto-selecionado: Comparação entre os gêneros. **Revista Brasileira de Cineantropometria e Desempenho Humano**, v. 11, n. 3, p. 307-313, 2009.
- LEICHT, A. S.; CROWTHER, R. G. Pedometer accuracy during walking over different surfaces. **Medicine and Science in Sports and Exercise**, v. 39, n. 10, p. 1847-1850, 2007.
- LOFTIN, M. M.; WADDELL, D. E.; ROBINSON, J. H.; OWENS, G. S. Comparison of energy expenditure to walk or run a mile in adult normal weight and overweight men and women. **Journal of Strength and Conditioning Research**, v. 24, n. 10, p. 2794-2798, 2010.
- MATSUDO, S.; ARAÚJO, T.; MATSUDO, V.; ANDRADE, D.; ANDRADE, E.; OLIVEIRA, L. C.; BRAGGION, G. Questionário internacional de atividade física (IPAQ): estudo de validade e reprodutibilidade no Brasil. **Revista Brasileira de Atividade Física e Saúde**, v. 6, n. 2, p. 5-18, 2001.
- McARDLE, W. D.; KATCH, F. I.; KATCH, V. L. **Exercise physiology: energy, nutrition and human performance**. Philadelphia: Lippincott Williams and Wilkins, 2006.
- MELLO, C. M.; TIRAPEGUI, J.; RIBEIRO, S. M. L. R. Gasto energético corporal: conceitos, formas de avaliação e sua relação com a obesidade. **Arquivos Brasileiros de Endocrinologia e Metabologia**, v. 52, n. 3, p. 452-464, 2008.
- PINTAR, J. A.; ROBERTSON, R. J.; KRISKA, A. M.; NAGLE, E.; GOSS, F. L. The influence of fitness and body weight on preferred exercise intensity. **Medicine and Science in Sports and Exercise**, v. 38, n. 5, p. 981-988, 2006.
- SIEGEL, P. Z.; BRACKBILL, R. M.; HEATH, G. W. The epidemiology of walking for exercise: implications for promoting activity among sedentary groups. **American Journal of Public Health**, v. 85, n. 5, p. 706-710, 1995.
- SIRI, W. E. Body composition from fluid spaces and density. In: BROZEK, J.; HENSCHER, A. (Ed.). **Techniques for measuring body composition**. Washington, D.C.: National Academy of Science, 1961. p. 223-244.
- SPELMAN, C. C.; PATE, R. R.; MACERA, C. A.; WARD, D. S. Self-selected exercise intensity of habitual walkers. **Medicine and Science in Sports and Exercise**, v. 25, n. 10, p. 1174-1179, 1993.
- WEIR, J. B. D. V. New methods for calculating metabolic rate with special reference to protein metabolism. **Journal of Physiology**, v. 109, n. 1, p. 1-9, 1949.

WILLIAMS, D. M.; DUNISGER, S.; CICCULO, J. T.; LEWIS, B. A.; ALBRECHT, A. E.; MARCUS, B. H. Acute affective response to a moderate intensity exercise stimulus predicts physical activity participation 6 and 12 months later. **Psychology in Sport and Exercise**, v. 9, n. 3, p. 231-245, 2008.

Received on February 3, 2010.

Accepted on April 4, 2011.

License information: This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.